Remarks

Claims 1, 2-4, and 7-11 have been amended. Claims 15, 18, 21, 44, 59, 70, and 77 have been cancelled without prejudice to their subsequent reintroduction into this application or their introduction into a related application. New claim 79 has been added. Upon entry of this paper, claims 1-14 and 79 will be pending and under consideration.

Support for the amendments can be found throughout the application as filed. For example, support for the amendment to claim 1 appears, for example, on page 25, line 25, in the paragraph bridging pages 33 and 34 and in Figures 2-6 of the application as filed. Support for the amendment to claim 7 can be found, for example, on page 25, line 25. Claims 2, 8 and 10 have been amended to recite that the first and second regions of the conduit are different. Support for the amendment can be found, for example, in Figures 2A and 2B and the associated text appearing on page 15 regarding elements **14** and **16**. In addition, claims 3, 4, 9 and 11 have been amended to modify the dependencies and/or grammar. Support for new claim 79 appears, for example, in claims 1 and 2 of the application as filed. Applicants believe that the aforementioned amendments introduce no new matter.

The undersigned attorney wishes to thank Examiner Bowers for his insightful comments during a telephonic interview with the undersigned and his colleague, Randall Morin, which took place on January 24, 2007. During the interview, the undersigned attorney and Examiner Bowers discussed the invention, the pending claims, the outstanding Office Action, the references applied in the Office Action, and the amendments to claim 1 appearing in this paper. The outstanding rejections are addressed in the order in which they appear in the Office Action.

Rejection Under 35 U.S.C. § 102(b) in view of Mahiout

According to Section 1 of the outstanding Office Action, claims 1-6 presently stand rejected under 35 U.S.C. § 102(b) as being anticipated by International Published Patent Application Serial Number WO 99/53322 by Mahiout ("Mahiout"). Applicants respectfully traverse this rejection to the extent that is maintained over the claims 1-6, as now amended, in view of the following remarks.

A "claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." See, MPEP § 2131. Applicants submit that Mahiout fails to meet this test.

Applicants submit that the Mahiout device is fundamentally different from the claimed invention. First, Mahiout describes the use of a device containing a test strip. In one embodiment (see, Figure 1 and Example 1), the device employs a "test strip" created within a capillary tube. In a second embodiment (see, Figure 2 and Example 2), the device is based on a paper test strip. During the interview, Examiner Bowers indicated that the embodiment of Example 1 of Mahiout was probably the most relevant to the present invention.

In Example 1 of Mahiout, the capillary tube is filled with beads referred to as "dried hydrophillic porous spherical material (200-500 μm)" (see, page 8 – Example 1). It appears that hemocyte (amebocyte) lysate is applied and dried on the polymeric powder (beads) (see, "Portion 1" on page 8). Afterwards, the beads with the lysate are placed within the capillary tube. Then, beads containing chromogenic substrate are introduced into a another region of the capillary tube next to portion 1 (see, "Portion 2" on page 8). The rest of the capillary tube is packed with beads containing other reagents to create the capillary tube shown in Figure 1.

Nowhere does Mahiout teach or suggest drying the lysate onto a fluid contacting surface of the capillary tube. In Mahiout, the lysate is applied to beads, which are then packed in the capillary tube. A fundamental feature of the cartridge of the claimed invention is that the lysate is dried on the fluid contacting surface of the conduit. Applicants submit that to pack the conduit of the cartridge of the claimed invention with such a powder would materially affect the flow characteristics and performance of the cartridge.

Furthermore, Mahiout describes a solid phase test for endotoxin, such as in a flat sheet or in a capillary form for detecting endotoxin in aqueous solutions. More particularly, the test device is a direct solid phase chromogenic assay. A test strip is wetted at the bottom with sample. Sample flows from the bottom to the top, and an indicator at the top develops a color that is indicative for the presence or absence of endotoxin in the sample. Accordingly, Mahiout

focuses entirely on providing an analytical test strip with a visual surface. It does not include any suggestion of alternatives to this format.

According to Mahiout, at the time of the invention a simple and quick method for determining endotoxin qualitatively in a test solution was sought in the art (see, for example, page 3, lines 3-4). In particular, from the second paragraph on page 1 to the second full paragraph on page 2, Mahiout sets forth prior methods for detecting endotoxin which are ultimately contrasted with Mahiout's invention, and describes the test strip as an advance over prior methods, such as optical absorption. Thus, Mahiout fails to teach or suggest (and even teaches away from) an optical cell, as described in Applicants' claim 1, and instead describes a visual surface (for example, in Figure 1).

In summary, Applicants submit that Mahiout fails to teach or suggest each and every element of independent claim 1, and the claims depending therefrom. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Rejection Under 35 U.S.C. § 102(b) in view of Numazawa

According to Section 2 of the outstanding Office Action, claims 1, 4-7 and 12-14 presently stand rejected under 35 U.S.C. § 102(b) as being anticipated by European Published Patent Application Serial Number EP 0121868 by Numazawa *et al.* ("Numazawa"). Applicants respectfully traverse this rejection, to the extent that is maintained over the claims, as now amended, in view of the following remarks.

As discussed previously, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. Applicants submit that Numazawa fails to meet this test.

Numazawa describes a transparent capillary tube for use in the detection of endotoxin. According to Numazawa, a transparent capillary tube format is advantageous because it obviates the need for transfer of a sample from a reaction vessel to a detection vessel (see, for example, the first full paragraph on page 2). Both Numazawa's capillary tube and the present invention are devices that perform both the reaction and detection aspects for testing endotoxin in a liquid

sample. However, Numazawa's capillary tube, as exemplified in Figures 1-4, is a transparent cylindrical tube with few component parts, namely endotoxin reagent **2** disposed within the tube (see, Figures 1-4), and, for example, an optional (i) colored portion **3** running along the length of the tube (see, Figure 2), (ii) suction member **4** attached to one end of the tube (see, Figure 3), and (iii) graduated scale **5**, disposed about the tube (see, Figure 4). Applicants submit that Numazawa fails to teach the cartridge of the claimed invention.

For example, the cartridge of independent claims 1 and 7 of the present invention comprise a housing that defines a fluid inlet port, an optical cell, and a conduit having a fluid contacting surface for providing fluid flow communication between the fluid inlet port and the optical cell. Numazawa fails to teach or suggest a cartridge comprising the separate components of an optical cell and a conduit. Rather, Numazawa describes a capillary - "reaction" - tube **1** with endotoxin reagent **2** sealed within tube **1** (see, for example, page 4, lines 14-18). The result is visualized along the entire length of the capillary tube, as exemplified in Figure 2, where the colored background runs the length of the capillary tube. In other words, there is no separate conduit and optical cell in Numazawa's capillary tube. In addition, Applicants have amended claim 1 to further specify that the optical cell is located downstream of the conduit. This is not possible in Numazawa's capillary tube as there is no separate conduit and optical cell. Therefore, the optical cell cannot be located downstream of the conduit, as is required by claim 1.

In addition, the cartridge of independent claims 1 and 7 requires, in part, that when a sample is applied to the fluid inlet port, the sample traverses the region of the fluid contacting surface having hemocyte lysate disposed thereon and solubilizes the hemocyte lysate during transport to the optical cell. However, with Numazawa's reaction tube, a sample is drawn into the tube by capillary action to dissolve the endotoxin reagent, and the tube is incubated, for example, heated, to facilitate the reaction between the sample and endotoxin reagent (see page 5, lines 8-19). Following the reaction, the reaction tube is tilted to observe gelation and any turbidometric or colorimetric changes indicative of the presence of endotoxin (see page 5, lines 19-26). Accordingly, the sample in Numazawa's reaction tube does not traverse the region

containing the lysate during transport to the optical cell, as required by claims 1 and 7 of the present invention.

In addition, independent claim 7 requires a housing defining a first fluid inlet port, a first optical cell, a first conduit, a second fluid inlet port, a second optical cell, and a second conduit. The Office Action indicates that Numazawa describes such a housing in Figure 7 and on page 10. Applicants respectfully submit that Figures 5 and 7 and pages 9 and 10 in Numazawa describe a hermetically sealed membrane for packaging one or more capillary reaction tubes, particularly open-ended reaction tubes, and that Numazawa fails to teach or suggest a housing defining inlet ports, optical cells and conduits. For the sake of argument only, even if one were to assume that Numazawa's membrane container is opened and that tests are performed using the multiple capillary reaction tubes while still disposed within the membrane container, the membrane container does not define fluid inlet ports, conduits, or optical cells, as is required by the housing of independent claim 7.

In summary, Applicants submit that Numazawa fails to teach or suggest each and every element of independent claims 1 and 7, and the claims depending therefrom. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Rejection Under 35 U.S.C. § 103

According to section 3 of the outstanding Office Action, claims 7-14 presently stand rejected under 35 U.S.C. § 103 as being obvious over Mahiout in view of either Numazawa or U.S. Patent Number 6,306,659 by Parce *et al.* ("Parce"). Page 6, second paragraph, of the Office Action appears to indicate that Numazawa or Parce are being applied to Numazawa to satisfy the limitation of a housing defining multiple, parallel inlet ports, optical cells, and conduits, as required in independent claim 7 of the present invention. Applicants respectfully traverse this rejection to the extent that it is maintained over claim 7, as amended, and the claims depending therefrom, in view of the following remarks.

With respect to the Office's apparent combination of Mahiout with Numazawa to satisfy the limitation of a housing defining multiple, parallel inlet ports, optical cells, and conduits, as required in independent claim 7, Applicant's reiterate that Figures 5 and 7 and pages 9 and 10 in Numazawa merely describe a sterile membrane container for packaging one or more capillary reaction tubes, particularly open-ended reaction tubes. Applicants submit that Numazawa fails to teach or suggest a housing defining multiple inlet ports, optical cells and conduits. Applicants submit that Numazawa fails to make up for the deficiencies in Mahiout. Accordingly, neither Mahiout nor Numazawa, alone or combination, teach or suggest the subject matter of amended claim 7, taken as a whole.

Furthermore, Applicants submit that there is no teaching or suggestion for the skilled artisan to modify the teachings of Mahiout as proposed by the Examiner or that, even if there was such motivation, that the resulting device would have a reasonable expectation of being operative.

With respect to the Office's apparent combination of Mahiout with Parce, Applicants respectfully submit that this combination fails to teach or suggest each and every element of amended claim 7, for example, the hemocyte lysate dried on a fluid contacting surface of the conduit. As noted above, Mahiout describes applying lysate to powder that is then packed in the capillary tube. Accordingly, the lysate is not dried on the fluid contacting surface of the capillary tube. Although Parce describes various microfluidic devices and microfluidic methods, Parce fails to disclose the incorporation of a hemocyte lysate in its devices. Accordingly, Applicants submit that the combined teachings of Mahiout and Parce fail to teach the claimed invention, taken as a whole.

Furthermore, as mentioned, Parce describes microfluidic devices and microfluidic methods. Applicants submit that the skilled artisan would not have been motivated to modify the device of Mahiout as proposed by the Examiner based on the microfluidic devices of Parce. Applicants submit that the skilled artisan having reviewed Parce would have no reason to modify the Mahiout device to include multiple fluid inlet ports, conduits or optical cells.

In view of the foregoing, Applicants respectfully request that the foregoing rejections be reconsidered and withdrawn.

Conclusion

Applicants believe that, in the view of the above amendments and comments, the pending claims are in condition for allowance. Early favorable action is respectfully solicited. The Office is invited to contact the undersigned with any questions about this submission.

Respectfully submitted,

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